



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Staley A. Brod

Serial No.: 08/844,731

Filed: April 21, 1997

For: METHODS OF TREATING
AUTOIMMUNE DISEASES USING TYPE
ONE INTERFERONS

Group Art Unit: 1647

Examiner: Jegatheesan Seharaseyon

Atty. Dkt. No.: CLFR:114US/ D-5716

CERTIFICATE OF MAILING
37 C.F.R. §1.8

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April 17, 2006
Date

David L. Parker

Mail Stop Appeal Brief - Patents

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants hereby submit this Appeal Brief in response to the Final Office Action dated June 13, 2005. The fee for filing this Appeal Brief is attached hereto. This Brief is filed pursuant to the Notice of Appeal mailed September 12, 2005. The date for filing the instant Brief is April 15, 2005 based on the receipt of the Notice of Appeal by the Patent and Trademark Office on September 15, 2005. A petition for a five-month extension under §1.136(a) and an Information Disclosure Statement are included herewith. The Commissioner is authorized to withdraw the appropriate fees from Fulbright & Jaworski L.L.P. Deposit Account No. 50-

1212/CLFR:114US. Please date stamp and return the enclosed postcard to evidence receipt of this document.



TABLE OF CONTENTS

I.	<u>REAL PARTIES IN INTEREST</u>	1
II.	<u>RELATED APPEALS AND INTERFERENCES</u>	1
III.	<u>STATUS OF THE CLAIMS</u>	1
IV.	<u>STATUS OF AMENDMENTS</u>	1
V.	<u>SUMMARY OF THE CLAIMED SUBJECT MATTER</u>	2
VI.	<u>GROUND OF REJECTION</u>	2
VII.	<u>ARGUMENT</u>	3
VIII.	<u>CLAIMS APPENDIX</u>	
IX.	<u>EVIDENCE APPENDIX</u>	
X.	<u>RELATED PROCEEDINGS APPENDIX</u>	



BRIEF ON APPEAL

I. REAL PARTIES IN INTEREST

The real party in interest is the Assignee, Research Development Foundation.

II. RELATED APPEALS AND INTERFERENCES

Appeal No. 1999-2502 regarding U.S. Application No. 08/631,470, of which the instant application is a continuation-in-part.

Appeal No. 1999-2508 regarding U.S. Application No. 08/844,731 (the instant application).

Appeal No. 2000-1094 regarding U.S. Application No. 08/946,710 which is a continuation-in-part of the instant application.

III. STATUS OF THE CLAIMS

Claims 1-7, 10, 12-15, 18 and 21-22 were previously canceled and thus claims 8-9, 11, 16-17, and 19-20 are currently pending in the case. The final rejection of claims 8-9, 11, 16-17 and 19-20 is the subject of the instant appeal. A copy of the appealed claims is attached hereto as Appendix 1.

IV. STATUS OF AMENDMENTS

Appellants are filing an amendment to the claims pursuant to 37 C.F.R. § 1.116 (b)(2) concurrently with this brief. Appellant believes that the amendment is entitled to entry under the standard set forth in MPEP §1207.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The instant application is directed to methods for treating autoimmune diseases with oral interferon. In particular, the independent claims that are the subject of the instant appeal are directed to a method of decreasing the incidence of insulin-dependent diabetes mellitus (IDDM) in at-risk populations (see page 8, lines 20-24 of the specification), a method of delaying the onset of insulin-dependent diabetes mellitus in at-risk populations (see page 20, line 23 through page 21, line 1) and a method of reducing blood glucose in a human (see original claims 12 and 15 on page 79 of the specification).

Each of the claimed methods of the instant invention involve oral administration of interferon (IFN) α (page 19, line 22 through page 20, line 2) in a dosage of 10,000 to 30,000 units (or International Units "I.U.") (page 59, lines 6-8 of the specification) which is immediately swallowed to be ingested (page 70, lines 3-5 of the specification). Interferon for use in these methods may be, for example, human recombinant interferon, rat interferon or murine interferon (page 20, lines 3-5). In certain instances, interferon may be administered to an individual every other day (see original claim 11 of page 79 of the specification).

VI. GROUND OF THE REJECTION

Claims 8, 9, 11, 16, 17, 19 and 20 have been rejected under 35 U.S.C. 103(a) as unpatentable over Sobel, U.S. Patent No: 5,780,021 (hereafter "Sobel") in view of Cummins, Jr., U.S. Patent No: 5,019,382 (here after "Cummins '382") and further in view of Cummins, Jr., U.S. Patent No: 4,462,985 (hereafter "Cummins '985").

VII. ARGUMENT

The Examiner has failed to set forth a *prima facie* case for obviousness in the rejection of the current claims. The rejection alleges that Sobel teaches the administration IFN- α for the prevention of IDDM and further that Cummins '985 teaches oral administration of interferon in a dosage range comprising the range recited in the claims 8, 16 and 19. The Examiner argues that there would have been motivation to use the dosage range of Cummins '985 with a reasonable expectation of success in view of the teachings of Cummins '382. However, in order to properly lodge an obviousness rejection and shift the burden to the Appellant, the Examiner must come forth with relevant material evidence that supports the allegations and such evidence must be sufficient to make a *prima facie* case. In the case of the instant rejections, the Examiner has failed to set forth sufficient evidence to make a *prima facie* case.

The first reference cited in the instant rejection, Sobel, concerns the treatment of IDDM however, Sobel does not teach or suggest the dose range of the instant claims. Indeed, Sobel teaches away from the claimed interferon dose ranges. For example, Sobel states that "Generally, in accordance with the present invention, the amount of single subtype of α -IFN or β -IFN, hybrids, analogs or mixtures thereof administered per dose either prior to or after the onset of disease is about 1×10^5 units to about 75×10^6 units with administrations being given from once per day to about once per week," (Column 4, lines 10-16). At the minimum this dose is over three times higher than that which is recited in the claims at issue. Sobel does not indicate or suggest that lower doses of interferon would be effective. In fact, analysis of the studies in figures 1 and 2 of Sobel indicates that when administered in a similar fashion 400,000 units of IFN was more effective at preventing IDDM than 100,000 units of IFN (compare the black diamonds from FIG. 1 and FIG. 2). Thus, a review of Sobel would suggest to one of skill in the

art that, if anything, higher doses of interferon might be preferred to treat IDDM. Thus, Sobel alone does not teach the oral IFN dose range of the claims nor does it suggest such a range.

Apparently, recognizing this deficiency in Sobel, the Examiner additionally cites Cummins '985 in the rejection. This reference concern the treatment of diseases that are not related to IDDM and thus the reference is not relevant to the instant invention. According, to Cummins '985, the "Dosage required for therapeutic effect are expected to vary widely depending on the mammal patient and condition treated, with from about 10 to about 1,000 units pre kg in unit dosage form is believed operative," (Column 9, lines 20-23). As noted by the Examiner, the dosage range of Cummins '985 comprises the range of the instant claims. **However, Cummins '985 does not concern the use of interferon for controlling or suppressing an autoimmune disease such as IDDM.** Rather, this reference concerns oral interferon administration **for enhancing immune response.** Activation of immune cells is far removed from, and in fact contrary to, the desired effect for treatment of IDDM, since IDDM is a "chronic disorder that results from autoimmune destruction [activated immune cells] of the insulin producing pancreatic b cell[s]," (pg. 4 lines 4-6 of the instant specification). In fact the dosage range proposed by Cummins '985 is based upon experiments involving treatment of benign papillomas, metastatic melanoma and metastatic breast cancer, all of which are conditions where enhanced immune response is desired. Thus, Cummins '985 describes dosage ranges of oral interferon that may be used in enhancing an immune response. In view of the immune enhancing effects taught by Cummins '985 one of skill in the art would not be motivated to combine the teachings of Sobel with the dosage range of Cummins '985 for the treatment of IDDM.

In a further attempt to overcome this deficiency, the Examiner additionally cites Cummins '382 which concerns the treatment of autoimmune diseases with low dose oral interferon. However, given that Cummins '985 does not concern the treatment of autoimmune disease it is not clear how this reference would provide a motivation to combine Sobel and Cummins '985. Cummins '382 does concern treatment of autoimmune disease however, the dose ranges disclosed therein are lower than those discussed in Cummins '985. These two references are by the same inventor and they teach different interferon dose ranges for use in treatment of different types of disease. When viewed together, these references would indicate to one of skill in the art that an interferon dose range effective to treat a particular disease will depend upon the disease type and thus the skilled artisan would not be motivated to combine the teachings of Sobel and Cummins '985 **especially in view of the teachings of Cummins '382**. Appellants, therefore assert that Cummins '382 does not provide a motivation to combine Cummins '985 and Sobel to arrive at the claimed dose of interferon for IDDM therapy.

Appellants furthermore point-out that Cummins '382 teaches oral interferon dose ranges that are an order of magnitude lower than those of the instant claims for treating autoimmune disease. Thus, in view of Cummins '382 one of skill in the art could not reasonably expect success using the higher dose ranges as recited in the claims. Specifically, Cummins '382 employs oral IFN dosages of about 0.01 to about 5 units per pound which is equivalent to about 19 to 953 units per individual for a male human (Column 4, lines 19-27). Not only is the dosage range taught by Cummins '382 much lower than the claimed dosage range, Cummins '382 suggests that preferred dosage ranges for treatment of autoimmune diseases are even lower. For example in column 4, lines 24- 32, Cummins '382 states:

Treatment of such disease is in accordance with the present invention comprises administering interferon at a dosage of 0.01 to about 5 IU/lb [1.9 to 952 I.U./average male American] per day in a dosage form adapted to promote contact of said dosage of interferon with the oral and pharyngeal mucosa of said animal. Preferably, the dosage of interferon is from 0.1 to about 4.0 IU/lb [19.0 to 762 I.U./average male American*] per day, more preferably 0.5 to about 1.5 IU/lb of body weight [95 to 285 I.U./average male American*] per day.*

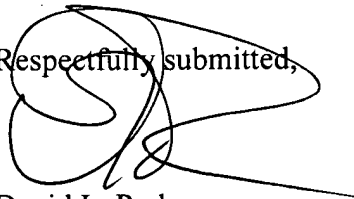
** All conversions based on the calculations from the March 11, 2005*

Response to Office Action.

Thus, Cummins '382 not suggest the using the high dose ranges of Cummins '985 rather, it teaches away from such ranges by suggesting that lower dose ranges are preferred. Thus, Cummins '382 does not suggest that the higher dose ranges of the instant claims would be effective for treating IDDM.

In view of the foregoing arguments, Appellants see no motivation or suggestion to combine the references cited by the Examiner. Rather, Appellants submit that the skilled artisan would certainly not expect success from combination to teachings of Sobel and Cummins '985. Therefore, the Examiner has failed to properly form a *prima facie* case for obviousness. It is respectfully submitted, that none of the pending claims are properly rejected under 35 U.S.C. §103. Appellants respectfully request that the Board reverse the pending grounds for rejection.

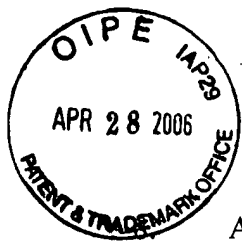
Respectfully submitted,



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Date: April 17, 2006



VIII. CLAIMS APPENDIX

A method of decreasing the incidence of insulin-dependent diabetes mellitus in at-risk populations:

orally administering 10,000 to 30,000 units of IFN- α to individuals of said at-risk population;
and

immediately swallowing to ingest said IFN- α , thereby decreasing the incidence of insulin-dependent diabetes mellitus in the at-risk populations.

9. The method of claim 8, wherein said interferon is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

11. The method of claim 8, wherein said interferon is administered every other day.

16. A method of delaying the onset of insulin-dependent diabetes mellitus in at-risk populations, comprising:

orally administering 10,000 to 30,000 units of IFN- α to individuals of said at-risk population;
and

immediately swallowing to ingest said IFN- α , thereby delaying the onset of insulin-dependent diabetes mellitus in the at-risk populations.

17. The method of claim 16, wherein said IFN- α is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

19. A method of reducing blood glucose levels in a human comprising:

orally administering 10,000 to 30,000 units of IFN- α to said human;

and immediately swallowing to ingest said IFN- α , thereby reducing blood glucose levels in said human.

20. The method of claim 19, wherein said interferon is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

IX. EVIDENCE APPENDIX

- Exhibit A: Final Office Action dated June 13, 2005
- Exhibit B: Sobel (U.S. Patent No. 5,780,021); cited in Office Action dated June 13, 2005
- Exhibit C: Cummins, Jr. (U.S. Patent No. 5,019,382); cited in Office Action dated June 13, 2005
- Exhibit D: Cummins, Jr. (U.S. Patent No. 4,462,985); cited in Office Action dated June 13, 2005
- Exhibit E: Response to Office Action dated March 11, 2005.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/844,731	04/21/1997	STALEY A. BROD	D5716-CIP3	7636
EXAMINER				
SEHARASEYON, JEGATHEESAN				
ART UNIT		PAPER NUMBER		
1647				

27851 7590 06/13/2005
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HOUSTON, TX 77071

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

2 mo. due to Provoked Advis
Action due: 8/13/05. Initial

RECEIVED
Date(s) Docketed: 9/13/05. Final deadline
12/13/05. Notice of Appeal
due 9/13/05. Final 12/13/05
JUN 27 2005
Client: CLFR:114US
Attorney(s): DLP, MPB
Initials: [Signature]



Office Action Summary

Application No.	Applicant(s)	
08/844,731	BROD, STALEY A.	
Examiner	Art Unit	
Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9,11,16,17,19 and 20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 8,9,11,16,17,19 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

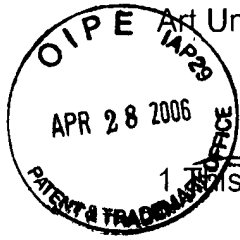
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/14/2005</u> | 6) <input type="checkbox"/> Other: _____ |

20

Art Unit: 1647



DETAILED ACTION

1. This office action is in response to the amendment and response filed on 3/14/05.

Applicant has cancelled claims 1-14. Claims 8, 16 and 19 have been amended. Claims 10, 18 and 21 have been cancelled. Thus, claims 8-9, 11, 16-17 and 19-20 are under consideration.

2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. The rejection of claims 8-11 and 16-18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. Specifically, Applicant has pointed out in the specification what an "at risk population" is.

Claim Rejections - 35 USC § 102

4. The rejection of claims 8, 9, 11, 16, 17, 19, 20 and 22 under 35 U.S.C. 102(e) as being anticipated by Sobel (U.S. Patent No: 5,780,021) is withdrawn because Sobel does describe the recited dosages of the instant invention.

5. New Rejections necessitated by Applicants amendments.

Claim Rejections - 35 USC § 103

6. The rejection of claims 10, 18 and 21 under 35 U.S.C. 103(a) as being unpatentable over Sobel (U.S. Patent No: 5,780,021) in view of Cummings (U.S. Patent No: 5, 019, 382) and Cummings (U.S. Patent No: 4, 497, 795) is withdrawn in favor of the rejection of claims 8-9, 11, 16-17 and 19-20 under 35 U.S.C. 103(a) as being unpatentable over

Art Unit: 1647

Sobel (U.S. Patent No: 5,780,021) in view of Cummings (U.S. Patent No: 5, 019, 382) and Cummings (U.S. Patent No: 4, 462, 985).

The rejection is withdrawn because Applicant has elected to cancel the claims. Sobel's teachings have been discussed in paragraph 2 of 03/08/2004 Office Action and above in paragraph 6 of 11/29/2004. The reference does not teach dosage ranges described in claims 8, 16 and 19. Cummings describes the administration of about 10 to 1,000 units per kg of body weight (see claim 7). Based on the body weight of 87 Kg (males) or 75 Kg (females) provided by the Applicant, this translates to 870 to 87,000 units or 750 to 75,000 units of interferon. This covers the dosage range recited in the claims 8, 16 and 19. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the interferon doses of Sobel to those taught by Cummings with expectation of treating IDMM patients. One of ordinary skill in the art would have been motivated to use interferon in the doses recommended by Cummings et al to treat IDMM with the expectation of success as because Cummings (U.S. Patent No: 5, 019, 382) teaches the treatment of autoimmune disorder, which includes IDMM. Therefore, the instant claims are *prima facie* obvious over Sobel (U.S. Patent No: 5,780,021) in view of Cummings (U.S. Patent No: 5, 019, 382) and Cummings (U.S. Patent No: 4, 497, 795).

7. No Claims are allowable.

Art Unit: 1647

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact information


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

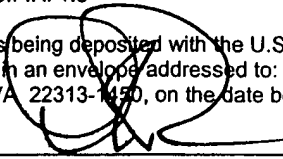
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

Art Unit: 1647

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 06/05


JANET ANDRES
PRIMARY EXAMINER

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March 11, 2005 Date	 David L. Parker

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Stanley A. Brod

Serial No.: 08/844,731

Filed: October 28, 2003

For: METHODS OF TREATING
AUTOIMMUNE DISEASE USING TYPE
ONE INTERFERONS

Group Art Unit: 1647

Examiner: Jegatheesan Seharaseyon

Atty. Dkt. No.: CLFR:114US/D5716

AMENDMENT AND RESPONSE TO OFFICE ACTION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is submitted in response to the Office Action dated November 29, 2004, for which the three-month date for response is February 28, 2005. No fees are believed due in connection with this paper. However, should any such fees become due consider this paragraph a request and authorization to withdraw the appropriate fee under 37 C.F.R. §§ 1.16 to 1.21 from *Fulbright & Jaworski, L.L.P.* Account No. 50-1212/CLFR:114US.

Reconsideration of the application is respectfully requested.

CLAIM AMENDMENTS

1-7. (Canceled)

8. (Currently amended) A method of decreasing the incidence of insulin-dependent diabetes mellitus in at-risk populations[[,]]:

oOrally administering 10,000 to 30,000 units of IFN- α to individuals of said at-risk population;
and

iImmediately swallowing to ingest said IFN- α , thereby decreasing the incidence of insulin-dependent diabetes mellitus in the at-risk populations.

9. (Previously presented) The method of claim 8, wherein said interferon is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

10. (Canceled)

11. (Previously presented) The method of claim 8, wherein said interferon is administered every other day.

12-15. (Canceled)

16. (Currently amended) A method of delaying the onset of insulin-dependent diabetes mellitus in at-risk populations, comprising:

oOrally administering 10,000 to 30,000 units of IFN- α to individuals of said at-risk population;
and

iImmediately swallowing to ingest said IFN- α , thereby delaying the onset of insulin-dependent diabetes mellitus in the at-risk populations.

17. (Previously presented) The method of claim 16, wherein said IFN- α is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

18. (Canceled)

19. (Currently amended) A method of reducing blood glucose levels in a human comprising:

oOrally administering 10,000 to 30,000 units of IFN- α to said human;

aAnd immediately swallowing to ingest said IFN- α , thereby reducing blood glucose levels in said human.

20. (Previously presented) The method of claim 19, wherein said interferon is selected from the group consisting of human recombinant interferon, rat interferon and murine interferon.

21-22. (Canceled)

RESPONSE TO OFFICE ACTION

A. Status of the Claims

The Action indicates that claims 8-11, and 16-22 are pending however Applicant notes that claim 22 was canceled in the Response dated May 19, 2004. Claims 8, 16 and 19 are amended herein, and claims 10, 18 and 21 have been canceled. Therefore, claims 8-9, 11, 16-17, and 19-20 are currently active in the application.

Support for amendments to claims 8, 16 and 19 can be found, at least on page 59 lines 6-8.

B. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 8-11 and 16-18 as being indefinite for failing to point out and distinctly claim the subject matter of the invention. Specifically, the Action asserts that the phrase “at-risk populations” has no limiting definition in the specification. Applicant respectfully traverses the rejection and notes “at-risk populations” is defined in the specification on page 75, lines 2 through 8. In view of the foregoing removal of the rejection is respectfully requested.

C. Rejection of Claims Under 35 U.S.C. §102(e)

The Action rejects claims 8, 9, 11, 16, 17, 19, 20, and 22 under 35 U.S.C. §102(e) as anticipated by Sobel (U.S. Patent No. 5,780,021). In response, Applicant observes that Sobel teaches a dose range of 100,000 to 10 million units (column 49, line 26) thus, Sobel can not anticipate the subject claims. Applicant respectfully requests that this rejection be withdrawn.

D. Rejection of Claims Under 35 U.S.C. §103a

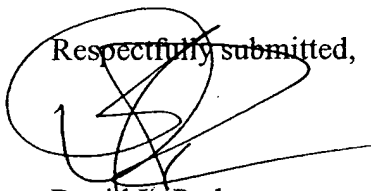
The Action rejects claims 10, 18 and 21 under U.S.C. §103(a) as being unpatentable over Sobel (U.S. Patent No. 5,780,021) in view of Cummings (U.S. Patent No. 5,019,382) and Cummings (U.S. Patent No. 4,497,795). Specifically the Action asserts that Sobel teaches oral administration of IFN- α for the treatment of diabetes, and that in view of Cummings ('382) and Cummings ('795) dosages of about 0.22 to 11 I.U./kg and about 500 to 5000 I.U./kg would be obvious to one of skill in the art.

In response, Applicant observes that the subject claims do not read on Sobel in view of Cummings ('382) and Cummings ('795). Considering the average weight of a human in the United States, about 191 lbs (86.6 kg) for males and 164 lbs (74.5 kg) for females as taught by Ogden *et al.* ("Mean body weight, height, and body mass index, United States 1960-2002," *Advance Data from Vital and Health Statistics*, No. 347 Oct. 27, 2004), a dosage range of about 0.22 to 11 I.U./kg, from Cummings '382, is equivalent to about 19 to 953 I.U./individual for males or 16 to 820 I.U./individual for females. Furthermore, applying the same conversions to the dose range of 500 to 5000 I.U./kg, from Cummins ('795) yields 43,300 to 433,000 I.U./individual for males and 37,300 to 373,000 I.U./individual for females. Thus, none of the dosages taught or fairly suggested by Sobel in view of Cummings ('382) and Cummings ('795) can be used to form a *prima facie* case for obviousness. In light of the foregoing, Applicant respectfully requests that this rejection be withdrawn.

E. Conclusion

In conclusion, Applicant submits that, in view of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested. If however, some unanswered questions remain in the mind of the Examiner, or if the Examiner would be available to discuss the merits of this case, and assist in facilitating its speedy allowance, the Examiner is invited to contact the Applicant's undersigned representative at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

A handwritten signature in black ink, appearing to be 'David L. Parker', is written over the words 'Respectfully submitted,'. The signature is stylized with a large, sweeping 'D' and 'P'.

David L. Parker
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X. RELATED PROCEEDINGS APPENDIX

Appeal No. 1999-2502 regarding U.S. Application No. 08/631,470, of which the instant application is a continuation-in-part.

Appeal No. 1999-2508 regarding U.S. Application No. 08/844,731 (the instant application).

Appeal No. 2000-1094 regarding U.S. Application No. 08/946,710 which is a continuation-in-part of the instant application.

5716 CIP
The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte STALEY A. BROD

Appeal No. 1999-2502
Application No. 08/631,470

ON BRIEF

MAILED

SEP 6 2002

PAT. & T.M. OFFICE
RECEIVED
SEP 6 2002
AND INTERFERENCES

Before WINTERS, WILLIAM F. SMITH, and GREEN, Administrative Patent
Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's
final rejection of claims 1-20. This appeal is related to Appeal Nos. 1999-2508
(Application No. 08/844,731) and 2000-1094 (Application No. 08/946,710).

Claims 1, 8, 13, and 19 are representative of the subject matter on
appeal, and read as follows:

1. A method of treating an auto-immune disease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested immediately upon oral administration.

8. A method of decreasing the severity or frequency of a relapse of multiple sclerosis in a human comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested immediately upon oral administration.

13. A method of reducing inflammation associated with an autoimmune disease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested after oral administration.

19. A method of decreasing the levels of a cytokine in an individual having multiple sclerosis, comprising the step of orally administering a type one interferon to said individual, wherein said cytokine is selected from the group consisting of TGF- β , IL-2, IL-10, IFN- γ and ICAM-1; and wherein said type one interferon is ingested immediately upon oral administration.

The examiner relies upon the following references:

Cummins, Jr. (Cummins) 5,019,382

May. 28, 1991

Shibutani et al. (Shibutani) "Toxicity Studies of Human Fibroblast Interferon Beta (I) Acute and Subacute Toxicity Studies in Mice and Rats," Iyakuhin Kenkyu, Vol. 18 (4), pp. 571-582 (1987)

Claims 1-12 and 19-20 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that applicant had possession of the claimed invention at the time of filing.

Claims 1-4, 6-11, and 13-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins, claims 5 and 12 stand rejected under 35 U.S.C.

§ 103(a) as obvious over the teachings of Cummins, and claims 1-20 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination

of Cummins and Shibutani. After careful review of the record and consideration of the issues before us, we affirm the rejection under 35 U.S.C. § 112, first paragraph, the rejection under 35 U.S.C. § 102(b) as it pertains to claims 1-3, 6-11, 13-15, and 17-19, and the rejection under 35 U.S.C. § 103(a) over Cummins of claims 5 and 12, but reverse the rejection under 35 U.S.C. § 102(b) as it pertains to claims 4, 16, and 20, and the rejection under 35 U.S.C. § 103(a) of claims 1-20 over the combination of Cummins and Shibutani.

BACKGROUND

The invention of the instant application is drawn to the treatment of autoimmune diseases in an animal, including humans, by orally administering a type one interferon to the animal. The interferon may be alpha or beta interferon, and is preferably human recombinant interferon, rat interferon, or murine interferon. See Specification, page 16.

According to the specification, the type one interferon is administered at a dosage that would effectively inhibit the onset or reoccurrence of an autoimmune disease. In addition, a wide variety of auto-immune diseases may be treated according to the invention, "includ[ing] multiple sclerosis, rheumatoid arthritis, diabetes mellitus, psoriasis, organ-specific auto-immune diseases, chronic inflammatory demyelinating polyradiculoneuropathy and Guillain-Barré syndrome." Id. at 17.

DISCUSSION

The panel would like to initially note that review of the issues on appeal was severely hampered by the lack of claim-by-claim analysis by the examiner, i.e., the use of "shotgun" rejections.

Findings of fact and the conclusions of law must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact relied upon in making the rejections are reviewed by the Court of Appeals for the Federal Circuit, or reviewing court, for substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). A determination of whether the findings of fact are supported by the record is difficult to make, however, if the examiner does not explicitly set forth those findings.

1. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-12, 19 and 20 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventor had possession of the claimed subject matter at the time of filing. Specifically, the examiner contends that there is no support that the interferon is ingested "immediately upon" oral administration. See Examiner's Answer, page 6.

Appellant asserts that the phrase "ingested immediately upon oral administration" is supported by the description of the animal experiments in the instant specification, wherein interferon was "administered directly to the distal esophagus, stomach and small intestine via a 20 gauge ball point needle." Appeal Brief, page 21.

Appellant appears to be arguing that the meaning of the limitation "ingest immediately" is that the interferon has little contact with the oral and/or pharyngeal mucosa, but rather is adsorbed by the distal esophagus, stomach and small and intestine. The specification, however, does not support such a

limited definition for ingest. Ingest, as used in common usage, means “[t]o take or absorb (food) into the body.” The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). See, e.g., Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1584 n.6, 39 USPQ2d 1573, 1578 n.3 (Fed. Cir. 1996) (noting that dictionary definitions may be relied upon in construing claim limitations “so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents”). The common usage of the term “ingest” does not exclude the adsorption by the oral and/or pharyngeal mucosa, and in fact, because the specification states that the α -interferon is to be administered orally, the skilled artisan, when reading the specification, would expect such adsorption.

Moreover, the examples relied upon by appellant as supporting the more limited definition of ingest does not contradict this finding, as the skilled artisan, would not interpret administration of interferon directly to the distal esophagus, stomach and small intestine via a 20 gauge ball point needle as oral administration. Thus, the skilled artisan would not immediately understand that “ingest” requires limiting contact with the oral and/or pharyngeal mucosa, and the rejection under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventor had possession of the claimed subject matter at the time of filing, is affirmed. See Purdue Pharma L.P. v. Faulding Pharmaceutical Co., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000).

2. Rejection under 35 U.S.C. § 102(b)

Claims 1-4, 6-11 and 13-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins. Due to its brevity, the entire rejection is set forth below.

See col. 4, lines 19-36, col. 5, lines 50-55, col. 6, lines 12-26, col. 13 [*sic*] [col. 12]¹ and the claims. Such disclosure meets the claims.

Examiner's Answer, page 4.

We initially note that our review was significantly hampered by the examiner's statement of the rejection. The examiner merely cited sections of the Cummins reference, without correlating the teachings of that reference to the requirements of each individual claim. This leaves appellant and the merits panel to surmise the examiner's position. In reviewing the record, however, appellant appears to be sufficiently apprised as to the examiner's position, and we thus proceed to a decision on the merits.² See In re Kronig, 539 F.2d 1300,

¹ The reference to column 13 in the rejection appears to be a typographical error. Appellant appears to recognize the error, as both the declaration and appellant's arguments are specifically directed to the example wherein a human multiple sclerosis patient was treated with alpha-interferon, which example appears at column 12 of Cummins.

² The fact that the issue is a rejection under section 102 of the statute allows us to proceed to the merits, because all the panel need determine is whether the reference discloses every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997).

1302-3, 190 USPQ 425, 426-7(CCPA 1976). We thus affirm the rejection as it applies to claims 1-3, 6-11, 13-15 and 17-19.³

Appellant argues that Cummins is not prior art because it is not enabled, and contends that two declarations, submitted during prosecution, support that position. Cummins, appellant asserts, presents one anecdotal example describing treatment of multiple sclerosis, and presents no examples for the treatment of human lupus erythematosus. In fact, appellant asserts, most of the diseases described by Cummins have no autoimmune basis, but are of viral origin and/or are veterinarian diseases. Appellant argues that the instant specification, however, "has targeted a much broader spectrum of auto-immune diseases including 27 cases of multiple sclerosis and 18 cases of treating autoimmune conditions in animals." Appeal Brief, page 9.

The one anecdotal example wherein multiple sclerosis was treated, according to appellant, involved a patient who received treatment for twenty-one days, and had no recurrence of neurologic symptoms for nine months. Appellant argues that the result is not surprising because multiple sclerosis is a highly variable disease with "unpredictable periods of remission and relapse." Id. at 10. In addition, appellant asserts that the Cummins patent does not have claims drawn to multiple sclerosis or other autoimmune diseases, "most likely because the data failed to enable such claims." Id.

³ Claims 4, 16 and 20 are treated separately because Appellant states that the claims do not stand or fall together, see Appeal Brief, page 6, and separately

Appellant also argues that Cummins cannot anticipate the instantly claimed invention because of differences in the route of administration of the interferon. The instant claims require that the type one interferon be "ingested immediately upon administration." According to appellant, Cummins requires that the interferon be administered in such a manner so as to have maximum contact with the oral and pharyngeal mucosa. Appellant argues that the instant claims require, citing the 132 declarations of Dr. Lindsey and Dr. Wolinsky, contact with the gastric and intestinal mucosa. In the human studies, appellant asserts, citing the declaration of Dr. Lindsey, that even though there was brief contact with the oral mucosa, the contact was minimal, unlike the contact taught by Cummins, where increased contact is sought. See id. at 13-14. Thus, Appellant contends that Cummins teaches away from the immediate ingestion of interferon, as required by the instant claims. See id. at 11-12.

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Glaug, 283 F.3d 1335, 1338, 62 USPQ2d 1151, 1153 (Fed. Cir. 2002). In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). During ex parte prosecution, however, claims are to be given their broadest reasonable interpretation consistent with

argues the patentability of those claims, see id. at 14-15.

the description of the invention in the specification. See In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

The Cummins reference states that human patients with conditions such as acute rheumatoid arthritis and multiple sclerosis were treated with human alpha-interferon at a dosage of 0.7 IU per pound twice a day. The interferon was retained in the mouth for one minute, and then either swallowed or discharged from the patient's mouth. See Cummins, Col. 12, lines 14-29.

With respect to the treatment of rheumatoid arthritis, an auto-immune disease, Cummins teaches that:

Two patients suffering from rheumatoid arthritis were treated—a Caucasian male age 44 and a Caucasian female age 44. The male patient was pain free in 7 days, and the female was pain free in 10 days. They were both continued on the oral interferon for 21 days total and have remained asymptomatic.

Col. 12, lines 30-35

With respect to the treatment of a patient with multiple sclerosis, Cummins states:

A 30-year-old Caucasian female nurse afflicted with multiple sclerosis and who had an extensive neurologic workup at City of Hope Hospital in Los Angeles received treatment in accordance with the present invention for 21 days. The patient has had no recurrence of her neurologic symptoms for the past nine months.

Col. 12, lines 40-45.

Thus, Cummins teaches all of the limitations of the claims. Cummins teaches a method of treating an auto-immune disease, such as rheumatoid arthritis or multiple sclerosis, through the administration of a type one interferon. Appellant's argument that the Cummins reference does not enable the present

claims because it presents a single anecdotal example is not found to be convincing. We recognize that in order for a reference to be anticipatory, it must be enabling. See In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962) ("[B]efore any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention."), In re Donohue, 766 F.2d 531, 533, 225 USPQ 619, 621 (Fed. Cir. 1985) (reaffirming LaGrice). However, Cummins clearly states that the symptoms of patients with rheumatoid arthritis and multiple sclerosis were reduced upon treatment of oral interferon. In addition, although appellant's specification may disclose auto-immune diseases not discussed or taught by Cummins, the disclosure of a species anticipates the genus. Cummins teaches the treatment of rheumatoid arthritis and multiple sclerosis, both auto-immune diseases. In addition, although appellant asserts that because Cummins does not claim the treatment of an auto-immune disease the examiner must have deemed such claims not to be enabled by the specification, appellant presents no evidence to that effect. Finally, just because appellant provides data that was not presented by Cummins does not render the Cummins reference nonenabling.

The declarations of John William Lindsey and Jerry S. Wolinski have been considered, but are also not deemed to be convincing. Both declarations address whether the claims at issue in this appeal would have been obvious over the Cummins reference. The issue is not one of obviousness, however, but anticipation. In addition, with respect to the comments that one would have not have had a reasonable expectation of success of practicing the claimed method, Cummins teaches at the very least that the treatment of rheumatoid arthritis

patients and a multiple sclerosis patient resulted in the reduction of symptoms, and thus does teach that the method produced the desired result—the treatment of an auto-immune disease.

Appellant's arguments and the statements in the declarations that Cummins cannot anticipate the method claims at issue because of the purported differences in the route of administration of the interferon have also been considered, but are also not deemed to be convincing. The declarations state that the method of Cummins stresses that contact with the oral and pharyngeal mucosa should be maximized, whereas the instant claims require that the interferon be "immediately ingested upon oral administration." As noted above, during examination, the claims are to be given their broadest reasonable interpretation. The specification provides no special meaning for the word "ingest." Ingest, however, may be defined as "[t]o take or absorb (food) into the body." The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). The definition of ingest, and the use of the phrase "such that the type one interferon is ingested immediately upon oral administration" does not exclude adsorption of the interferon through the oral and/or pharyngeal mucosa as taught by Cummins. Thus, the claims are not limited to a method of delivery wherein contact with the oral or pharyngeal mucosa is avoided.

Appellant also argues that dosages used by Cummins are smaller than the dosages required by the instant invention. Cummins, according to Appellant, administered dosages ranging from 0.01 to 5 I.U. per day, whereas the instant application uses dosages ranging from 5 I.U./kg to about 50,000 I.U./kg.

That argument is not found to be convincing with respect to those claims wherein no dosage is recited, i.e., claims 1-3, 6-10, 13-15, 18, and 19. With respect to claim 11, wherein a dosage of "from about 5 I.U./kg to 50,000 I.U./kg"

is recited, that dosage corresponds to a dosage of 2.3 I.U./lb to 23,000 I.U./lb, see Appeal Brief, page 14, thus two dosages of 7 I.U./lb falls within the range recited, and the rejection is affirmed. The rejection with respect to claims 4, 16 and 20 is reversed, however, as the lower end of the range, i.e., 50 I.U./kg (Claims 4 and 16) and 166 I.U./ kg (Claim 20), is higher than the dosage used by Cummins.

3. Rejection under 35 U.S.C. § 103(a) over Cummins

With respect to the rejection of claims 5 and 12 as being rendered obvious by Cummins, the examiner states:

The disclosure is the same as above as discussed for claims 1 and 8. The patent does not disclose an alternate day dosing. However, it does show that a daily dosage is possible, as a single dose or as divided and administered in a multiple daily dose regimen. The reference also teaches a staggered regimen of 1-3 days per week or month as an alternative to daily dosing. See col. 5, lines 50-55. With such a flexibility as taught by the reference, and since it is common knowledge in the art to employ such a regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc., it would have been obvious to one of ordinary skill in the art to adopt an alternate day dosing and administer [interferon] as shown by Cummins for [multiple sclerosis].

Examiner's Answer, pages 4-5.

The portion of the Cummins patent relied upon by the examiner states that:

Daily dosage of interferon can be administered as a single dose or, preferably, it is administered in a multiple-dose daily regimen. A staggered regimen, for example one to three days of treatment per week or month, can be used as an alternative to continuous daily treatment.

Col. 5, lines 51-56.

Appellant argues that the first portion of the above passage teaches a multiple-dose regimen rather than an alternate day regimen. In addition, according to appellant, although Cummins discloses a regimen of one to three days per week or month, that dosing regimen is also "alluded" by Cummins a being a less preferred mode of administration. The specific spacing of treatments is not discussed by Cummins, and thus, appellant contends that it is unclear whether this section refers to three continuous days of treatment, followed by a period without treatment, or single days of treatment separated by days without treatment. See Appeal Brief, pages 15-17. Thus, appellant concludes that the section relied upon by the examiner is non-enabling, as "[u]ndue experimentation would be necessary to try the other possible combinations days on therapy versus days off therapy." Id. at 17.

Appellant's arguments are not deemed to be convincing. Cummins teaches a variety of different treatment regimens, from daily to monthly. From those teachings, the ordinary artisan would have concluded that the spacing of the interferon treatments is not crucial to the success of the treatment method. "All the disclosures in a reference must be evaluated, including nonpreferred embodiments, ... and a reference is not limited to the disclosure of specific working examples." In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 199 (CCPA 1972) (citations omitted). As the examiner notes, and appellant does not refute, it is common in the art to use alternate day dosing, and it is irrelevant that such alternate dosing schedules may have been less preferred mode of administration.

In addition, merely because Cummins does not explicitly disclose alternate day dosing does not lead to the conclusion that the reference is not enabled for such dosing. As noted above, alternate day dosing is commonly

used in the art, and given the variety of dosing schedules taught by Cummins, the ordinary artisan would have had a reasonable expectation of success that such an alternate day dosing could be used in the treatment method taught by Cummins.

4. Rejection under 35 U.S.C. § 103(a) over Cummins and Shibanti

Claims 1-20 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins and Shibutani. The entire rejection is set forth in its entirety below.

The disclosure for the patent is as discussed above. The whole range of dosages claimed by the instant invention is not shown. However, the Shibutani abstract indicates that IFN toxicity studies with rats showed that it was tolerated well. Therefore, it would have been obvious to one of ordinary skill in the art to administer dosages higher than that shown in the patent with the reasonable expectation that such doses would not produce toxicity side-effects in humans. It would also have been obvious to employ such an alternate day dose regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc.

Examiner's Answer, page 5.

Again, the panel would like note that the examiner has entered a shotgun rejection of all of the claims, rather than performing a claim-by-claim analysis. The only claims that require a specific range of dosages are 4, 11, 16, and 20, and the rejection is only analyzed as it applies to those claims.

Appellant argues that the declarations filed under 37 CFR § 1.132 discuss the issue of dosage. According to appellant, the dosages found to be the most effective in the instant application do not overlap the dosages taught by

Cummins, and in fact, are two orders of magnitude greater than those used by Cummins.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Alton, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). In assessing the prior art, each prior art reference must be considered in its entirety in an obviousness determination. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). In assessing the teachings of the prior art reference as a whole, the examiner must also consider those disclosures that may teach away from the invention. See In re Fine, 837 F.3d 1071, 1074, 5 USPQ2d 1596, 1598 (1988).

In this case, Cummins teaches that the amount of interferon should be used in amounts of "less than 5 IU/lb of body weight," Col. 3, lines 9-12, and characterizes the method as "using interferon in low oral dosages," Col. 1, lines 6-14. Thus, Cummins teaches away from using higher dosages, and thus there is no motivation for increasing the dosage amount of interferon. Thus, the examiner has not set forth a prima facie case of obviousness, and the rejection over the combination of Cummins and Shibutani is reversed.

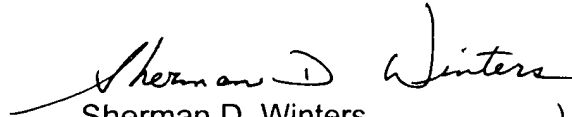

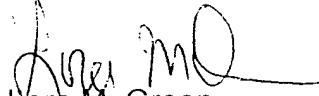
CONCLUSION

The rejections under 35 U.S.C. § 112, first paragraph, 35 U.S.C. § 102(b) as it pertains to claims 1-3, 6-11, 13-15, and 17-19, and 35 U.S.C. § 103(a) over

Cummins of claims 5 and 12 are affirmed. The rejections under 35 U.S.C. § 102(b) as it pertains to claims 4, 16, and 20, and 35 U.S.C. § 103(a) of claims 1-20 over the combination of Cummins and Shibutani, however, are reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; REVERSED-IN-PART

)	
Sherman D. Winters)	
Administrative Patent Judge)	
)	
)	BOARD OF PATENT
William F. Smith)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
Lora M. Green)	
Administrative Patent Judge)	

LG/dym

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7-716 000-
The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

Paper No. 12

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte STALEY A. BROD

MAILED

Appeal No. 1999-2508
Application No. 08/844,731

SEP - 6 2002

ON BRIEF

PAT. & T.M. OFFICE
AND OF APPEALS
AND INTERFERENCES

Before WINTERS, WILLIAM F. SMITH, and GREEN, Administrative Patent
Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's
final rejection of claims 1-18. We would like to note that this appeal is related to
Appeal Nos. 1999-2502 (Application No. 08/631,470) and 2000-1094
(Application No. 08/946,710), and that the claims at issue are identical to the
claims at issue in Appeal No. 2000-1094.

Claims 1, 8, 12, and 16 are representative of the subject matter on appeal, and read as follows:

1. A method of treating an auto-immune disease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested after oral administration.
8. A method of decreasing the incidence of insulin-dependent diabetes mellitus in at-risk populations, comprising the step of orally administering IFN- α to individuals of said at-risk population.
12. A method of reducing blood glucose levels in an animal comprising the step of orally administering IFN- α to said animal such that the IFN- α is ingested after oral administration.
16. A method of decreasing the onset of insulin-dependent diabetes mellitus in at-risk populations, comprising the step of orally administering IFN- α to individuals of said at-risk populations.

The examiner relies upon the following references:

Cummins, Jr. (Cummins)	5,019,382	May. 28, 1991
Sobel (abstract only)	WO94, 20122	Sept. 15, 1994

Shibutani et al. (Shibutani) "Toxicity Studies of Human Fibroblast Interferon Beta (I) Acute and Subacute Toxicity Studies in Mice and Rats," Iyakuhin Kenkyu, Vol. 18 (4), pp. 571-582 (1987)

Gross et al. (Gross) "Interferon- α with Condylomata acuminata and Juvenile Diabetes Mellitus," Deutsche Medizinische Wochenschrift, Vol. 111 (36), pp. 1351-1355, (1986) (abstract only)

Giron et al. (Giron) "Effect of Interferons and Poly(I): Poly (C) on the Pathogenesis of the Diabetogenic Variant of Encephalomyocarditis Virus in Different Mouse Strains," Journal of Interferon Research, Vol. 8 pp. 745-753 (1988) (abstract only)

Claims 1-4, 6, and 7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins, claim 5 stands rejected under 35 U.S.C. § 103(a) as obvious over the teachings of Cummins, and claims 1-18 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins, Shibutani and the abstracts of Sobel, Giron and Gross. In addition, claims 1-7 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of copending application 08/631,470 (the '470 application), and claims 8-18 are the subject of a provisional double-patenting rejection over claims 1-18 of the '470 application in view of the abstracts of Sobel, Gross and Giron. After careful review of the record and consideration of the issues before us, we affirm the rejection under 35 U.S.C. § 102(b) as to claims 1-3, 6, and 7, the rejection of claim 5 under 35 U.S.C. § 103(a) over Cummins, the provisional rejection under 35 U.S.C. § 101, and the provisional obviousness-type double-patenting rejection, but reverse the rejection under 35 U.S.C. § 102(b) as to claim 4. In addition, we vacate the rejection of claims 1-18 under 35 U.S.C. § 103(a) over the combination of Cummins, Shibutani, and the abstracts of Sobel, Gross and Giron.

BACKGROUND

The invention of the instant application is drawn to the treatment of autoimmune diseases in an animal, including humans, by orally administering a type one interferon to the animal. The interferon may be alpha or beta interferon, and is preferably human recombinant interferon, rat interferon, or murine interferon. See Specification, pages 19-20.

According to the specification, the type one interferon is administered at a dosage that would effectively inhibit the onset or reoccurrence of an autoimmune disease. In addition, a wide variety of auto-immune diseases may be treated according to the invention, "includ[ing] multiple sclerosis, rheumatoid arthritis, diabetes mellitus, psoriasis, organ-specific auto-immune diseases, chronic inflammatory demyelinating polyradiculoneuropathy and Guillain-Barré syndrome." Id. at 20.

DISCUSSION

The panel would like to initially note that review of the issues on appeal was severely hampered by the lack of claim-by-claim analysis by the examiner, i.e., the use "shot-gun" rejections.

Findings of fact and the conclusions of law must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact relied upon in making the rejections are reviewed by the Court of Appeals for the Federal Circuit, or reviewing court, for substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). A determination of whether the findings of fact are supported by the record is difficult to make, however, if the examiner does not explicitly set forth those findings.

1. Rejection under 35 U.S.C. § 102(b)

Claims 1-4, 6, and 7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins. Due to its brevity, the entire rejection is set forth below.

See col. 4, lines 19-36, col. 5, lines 50-55, col. 6, lines 12-26, col. 13 [sic] [col. 12]¹ and the claims. Such disclosure meets the claims.

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We initially note that our review was significantly hampered by the examiner's statement of the rejection. The examiner merely cited sections of the Cummins reference, without correlating the teachings of that reference to the requirements of each individual claim. This leaves appellant and the merits panel to surmise the examiner's position. In reviewing the record, however, appellant appears to be sufficiently apprised as to the examiner's position, and we thus proceed to a decision on the merits.² See In re Kronig, 539 F.2d 1300, 1302-3, 190 USPQ 425, 426-7(CCPA 1976). We thus affirm the rejection as it applies to claims 1-3, 6 and 7.³

Appellant argues that Cummins is not prior art because it is not enabled, and that two declarations, submitted during prosecution, support that position.

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³ Claim 4 is treated separately because Appellant states that the claims do not stand or fall together, see Appeal Brief, page 6, and separately argues the patentability of that claim, see id. at 16-17.

Cummins, appellant asserts, presents one anecdotal example describing treatment of multiple sclerosis, and presents no examples for the treatment of human lupus erythematosus. In fact, appellant asserts, most of the diseases described by Cummins have no autoimmune basis, but are of viral origin and/or are veterinarian diseases. Appellant argues that the instant specification, however, "has targeted a much broader spectrum of auto-immune diseases including 27 cases of multiple sclerosis, four cases of rheumatoid arthritis, and 18 cases of treating autoimmune conditions in animals." Appeal Brief, page 9.

The one anecdotal example wherein multiple sclerosis was treated, according to appellant, involved a patient who received treatment for twenty-one days, and had no recurrence of neurologic symptoms for nine months. Appellant argues that the result is not surprising because multiple sclerosis is a highly variable disease with "unpredictable periods of remission and relapse." Id. at 10. In support of his assertion that the Cummins reference is not enabling for the treatment of auto-immune diseases such as rheumatoid arthritis and multiple sclerosis, appellant further points out that the Cummins patent does not have claims drawn to multiple sclerosis or other autoimmune diseases. See id. at 9.

Appellant also argues that Cummins cannot anticipate the instantly claimed invention because of differences in the route of administration of the interferon. The instant claims require that the type one interferon be "ingested after administration." According to appellant, Cummins requires that the interferon be administered in such a manner so as to have maximum contact

with the oral and pharyngeal mucosa. Appellant argues that the instant claims require, citing the 132 declarations of Dr. Lindsey and Dr. Wolinsky, contact with the gastric and intestinal mucosa. In the human studies, appellant asserts, citing the declaration of Dr. Lindsey, that even though there was brief contact with the oral mucosa, the contact was minimal, unlike the contact taught by Cummins, where increased contact is sought. Thus, Appellant contends that Cummins teaches away from the immediate ingestion of interferon, as required by the instant claims. See id. at 12-15.

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Glaug, 283 F.3d 1335, 1338, 62 USPQ2d 1151, 1153 (Fed. Cir. 2002). In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). During ex parte prosecution, however, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification. See In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

The Cummins reference states that human patients with conditions such as acute rheumatoid arthritis and multiple sclerosis were treated with human alpha-interferon at a dosage of 0.7 IU per pound twice a day. The interferon was retained in the mouth for one minute, and then either swallowed or discharged from the patient's mouth. See id. at Col. 12, lines 14-29.

With respect to the treatment of rheumatoid arthritis, an auto-immune disease, Cummins teaches that:

Two patients suffering from rheumatoid arthritis were treated—a Caucasian male age 44 and a Caucasian female age 44. The male patient was pain free in 7 days, and the female was pain free in 10 days. They were both continued on the oral interferon for 21 days total and have remained asymptomatic.

Col. 12, lines 30-35.

With respect to the treatment of a patient with multiple sclerosis, Cummins states:

A 30-year-old Caucasian female nurse afflicted with multiple sclerosis and who had an extensive neurologic workup at City of Hope Hospital in Los Angeles received treatment in accordance with the present invention for 21 days. The patient has had no recurrence of her neurologic symptoms for the past nine months.

Col. 12, lines 40-45.

Thus, Cummins teaches all of the limitations of the claims. Cummins teaches a method of treating an auto-immune disease, such as rheumatoid arthritis or multiple sclerosis, through the administration of a type one interferon. Appellant's argument that the Cummins reference does not enable the present claims because it presents a single anecdotal example is not found to be convincing. We recognize that in order for a reference to be anticipatory, it must be enabling. See In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962) ("[B]efore any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention."), In re Donohue, 766 F.2d 531, 533, 225 USPQ 619, 621 (Fed. Cir. 1985) (reaffirming LaGrice). However, Cummins clearly states that the symptoms of patients with rheumatoid arthritis and multiple

sclerosis were reduced upon treatment of oral interferon. In addition, although appellant's specification may disclose auto-immune diseases not discussed or taught by Cummins, the disclosure of a species anticipates the genus. Cummins teaches the treatment of rheumatoid arthritis and multiple sclerosis, both auto-immune diseases. In addition, although appellant asserts that because Cummins does not claim the treatment of an auto-immune disease, the examiner must have deemed such claims not to be enabled by the specification, appellant presents no evidence to that effect. Finally, just because appellant provides data that was not presented by Cummins does not render the Cummins reference nonenabling.

The declarations of John William Lindsey and Jerry S. Wolinski have been considered, but are also not deemed to be convincing. Both declarations address whether the claims at issue in this appeal would have been obvious over the Cummins reference. The issue is not one of obviousness, however, but anticipation. In addition, with respect to the comments that one would have not have had a reasonable expectation of success of practicing the claimed method, Cummins teaches at the very least that the treatment of rheumatoid arthritis patients and a multiple sclerosis patient resulted in the reduction of symptoms, and thus does teach that the method produced the desired result—the treatment of an auto-immune disease.

Appellant's arguments and the statements in the declarations that Cummins cannot anticipate the method claims at issue because of the purported difference in the route of administration of the interferon have also been considered, but are also not deemed to be convincing. The declarations state that the method of Cummins stresses that contact with the oral and pharyngeal mucosa should be maximized, whereas the instant claims require that the

interferon be "ingested after oral administration." As noted above, during examination, the claims are to be given their broadest reasonable interpretation. The specification provides no special meaning for the word "ingest." Ingest, however, may be defined as "[t]o take or absorb (food) into the body." The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). The definition of ingest, and the use of the phrase "such that the type one interferon is ingested after oral administration" does not exclude adsorption of the interferon through the oral and/or pharyngeal mucosa as taught by Cummins. Thus, the claims are not limited to a method of delivery wherein contact with the oral or pharyngeal mucosa is avoided.

Appellant also argues that dosages used by Cummins are smaller than the dosages required by the instant invention. Cummins, according to Appellant, administered dosages ranging from 0.01 to 5 I.U. per day, whereas the instant application uses dosages ranging from 5 I.U./kg to about 50,000 I.U./kg.

This argument is not found to be convincing with respect to those claims wherein no dosage is recited, i.e., claims 1-3, 6, and 7. The rejection with respect to claim 4 is reversed, however, as the lower end of the range, i.e., 50 I.U./kg, is higher than the dosage used by Cummins.

2. Rejection under 35 U.S.C. § 103(a) over Cummins

With respect to the rejection of claim 5 as being rendered obvious by Cummins, the examiner states:

The disclosure is the same as above as discussed for claim 1. The patent does not disclose an alternate day dosing. However, it does show that a daily dosage is possible, as a single dosage or as divided and administered in a multiple daily dose regimen. The reference also teaches a staggered regimen of 1-3 days per week or month as an alternative to daily dosing. See col. 5, lines 50-55. With such a flexibility as taught by the reference, and since it is common knowledge in the art to employ such a regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc., it would have been obvious to one of ordinary skill in the art to adopt an alternate day dosing and administer [interferon] as shown by Cummins for [multiple sclerosis].

Examiner's Answer, pages 4-5.

The portion of the Cummins patent relied upon by the examiner states that:

Daily dosage of interferon can be administered as a single dose or, preferably, it is administered in a multiple-dose daily regimen. A staggered regimen, for example one to three days of treatment per week or month, can be used as an alternative to continuous daily treatment.

Col. 5, lines 51-56.

Appellant argues that the first portion of the above passage teaches a multiple-dose regimen rather than an alternate day regimen. In addition, according to appellant, although Cummins discloses a regimen of one to three days per week or month, that dosing regimen is also "alluded" by Cummins a being a less preferred mode of administration. The specific spacing of treatments is not discussed by Cummins, and thus, appellant contends that it is unclear whether this section refers to three continuous days of treatment,

followed by a period without treatment, or single days of treatment separated by days without treatment. See Appeal Brief, pages 18-19. Thus, appellant concludes that the section relied upon by the examiner is non-enabling, as “[u]ndue experimentation would be necessary to try the other possible combinations days on therapy versus days off therapy.” Id. at 20.

Appellant’s arguments are not deemed to be convincing. Cummins teaches a variety of different treatment regimens, from daily to monthly. From those teachings, the ordinary artisan would have concluded that the spacing of the treatments is not crucial to the success of the treatment method. “All the disclosures in a reference must be evaluated, including nonpreferred embodiments, ... and a reference is not limited to the disclosure of specific working examples.” In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 199 (CCPA 1972) (citations omitted). As the examiner notes, and appellant does not refute, it is common in the art to use alternate day dosing, and it is irrelevant that such alternate dosing schedules may have been less preferred mode of administration.

In addition, merely because Cummins does not explicitly disclose alternate day dosing does not lead to the conclusion that the reference is not enabled for such dosing. As noted above, alternate day dosing is commonly used in the art, and given the variety of dosing schedules taught by Cummins, the ordinary artisan would have had a reasonable expectation of success that such an alternate day dosing could be used in the treatment method taught by Cummins.

3. Rejection under 35 U.S.C. § 103(a) over Cummins, Shibanti and the Abstracts of Sobel, Gross, and Giron

Claims 1-18 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins, Shibutani, and the abstracts of Sobel, Gross and Giron. The entire rejection is set forth below.

The disclosure for the patent is as discussed above. The whole range of dosages claimed by the instant invention is not shown. However, the Shibutani abstract indicates that IFN toxicity studies with rats showed that it was tolerated well. Therefore it would have been obvious to one of ordinary skill in the art to administer dosages higher than that shown in the patent with the reasonable expectation that such doses would not produce toxicity side-effects in humans. It would also have been obvious to employ such an alternate day dose regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc. The references also do not disclose the prevention or treatment of diabetes. However, in view of the disclosure of the abstracts that show that it was already known in the art at the time the invention was made that interferon prevented the onset of diabetes, the subject matter as a whole would have been obvious to the person of ordinary skill in the art at the time the invention was filed.

Examiner's Answer, pages 5-6.

Again, the panel would like note that the examiner has entered a shotgun rejection of all of the claims, rather than performing a claim-by-claim analysis. The examiner relies upon Shibutani as a teaching dosage amounts over those taught by Cummins may be used, but dosage amounts are only specifically recited in claims 4, 10, 14, and 18. Moreover, the record is incomplete because the examiner failed to consider the Sobel, Giron and Gross references in their entireties.

Because of the lack of claim-by-claim analysis, and because the rejection did not consider the teachings the Sobel, Gross and Giron references in their entireties, and because it is the opinion of the panel that the Sobel reference, when considered in its entirety, may be relevant to the patentability of the claims, the obviousness rejection over Cummins, Shibutani and the abstracts of Sobel, Gross and Giron is vacated. See, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (stating that for meaningful judicial review to occur, the agency must present a full and reasoned explanation of its decision.).

As a final note, in assessing the prior art, each prior art reference must be considered in its entirety in an obviousness determination. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). In assessing the teachings of the prior art reference as a whole, the examiner must also consider those disclosures that may teach away from the invention. See In re Fine, 837 F.3d 1071, 1074, 5 USPQ2d 1596, 1598 (1988). In this case, Cummins teaches that the amount of interferon should be used in amounts of "less than 5 IU/lb of body weight," Col. 3, lines 9-12, and characterizes the method as "using interferon in low oral dosages," Col. 1, lines 6-14. Thus, Cummins may teach away from using higher dosages, and thus there may be no motivation for increasing the dosage amount of interferon. Thus, Cummins may teach away from a combination that includes Shibutani.

4. Provisional Rejection under 35 U.S.C. § 101

Claims 1-7 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as claims 1-7 of the '470 application.

Appellant states that should either application be allowed, claims 1-7 of the instant application will be canceled. As appellant has not presented any arguments as to why the rejection is improper, it is affirmed.

5. Obviousness Double Patenting rejection

Claims 8-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the '470 application in combination with the abstracts of Sobel, Gross and Giron. Appellant states that should either application be allowed, a terminal disclaimer will be filed. Again, as appellant has not presented any arguments as to why the rejection is improper, it is affirmed.

OTHER MATTERS

The Sobel reference, when considered in its entirety, appears to be relevant to the patentability of the claims at issue. Sobel teaches that autoimmune diseases, such as Type I diabetes mellitus, may be treated or prevented by the administration of an α -interferon or a β -interferon. See Sobel, page 1. Sobel teaches the use of different dosages and different administration schedules, and notes that any mammal may be treated, including humans. See id. at 7-8. In addition, Sobel teaches that the interferon may be administered orally. See id. at 8 and 26. Thus, upon receipt of the application, the examiner

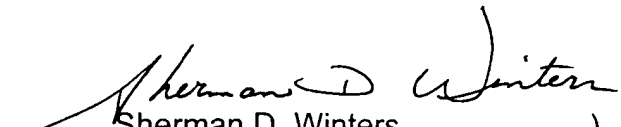
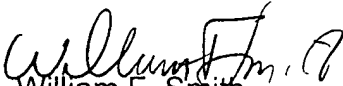
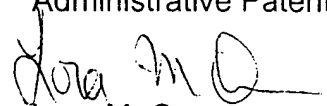
may want to consider the patentability of the claims in view of the teaching of Sobel.

CONCLUSION

The rejection under 35 U.S.C. 102(b) as to claims 1-3, 6, and 7, the rejection of claim 5 under 35 U.S.C. § 103(a) over Cummins, the provisional rejection under 35 U.S.C. § 101, and the provisional obviousness-type double-patenting rejection, are affirmed. The rejection under 35 U.S.C. § 102(b) as to claim 4, however, is reversed. In addition, we vacate the rejection of claims 1-18 under 35 U.S.C. § 103(a) over the combination of Cummins, Shibutani, and the abstracts of Sobel, Gross and Giron. Finally, the examiner may want to consider the patentability of the claims at issue in the appeal over the teachings of the Sobel reference in its entirety.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; REVERSED-IN-PART; VACATED-IN-PART

)	
Sherman D. Winters)	
Administrative Patent Judge)	
)	BOARD OF PATENT
William F. Smith)	
Administrative Patent Judge)	APPEALS AND
)	INTERFERENCES
Lora M. Green)	
Administrative Patent Judge)	

LG/dym

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5-716 CUPP

The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

Paper No. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte STALEY A. BROD

Appeal No. 2000-1094
Application No. 08/946,710

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GREEN, Administrative Patent
Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-18. We would like to note that this appeal is related to Appeal Nos. 1999-2502 (Application No. 08/631,470) and 1999-2508 (Application No. 08/844,731), and that the claims at issue are identical to the claims at issue Appeal. No. 1999-2508.

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PATENT OFFICE
UNITED STATES DEPT. OF COMMERCE
AND INTERFERENCES

Claims 1, 8, 12, and 16 are representative of the subject matter on appeal, and read as follows:

1. A method of treating an auto-immune disease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested after oral administration.
8. A method of decreasing the incidence of insulin-dependent diabetes mellitus in at-risk populations, comprising the step of orally administering IFN- α to individuals of said at-risk population.
12. A method of reducing blood glucose levels in an animal comprising the step of orally administering IFN- α to said animal such that the IFN- α is ingested after oral administration.
16. A method of decreasing the onset of insulin-dependent diabetes mellitus in at-risk populations, comprising the step of orally administering IFN- α to individuals of said at-risk populations.

The examiner relies upon the following references:

Cummins, Jr. (Cummins)	5,019,382	May. 28, 1991
Sobel (Sobel I)	5,624,895	Apr. 29, 1997
Sobel (Sobel II) (abstract only)	WO 94/20122	Sept. 15, 1994

Shibutani et al. (Shibutani) "Toxicity Studies of Human Fibroblast Interferon Beta (I) Acute and Subacute Toxicity Studies in Mice and Rats," Iyakuhin Kenkyu, Vol. 18 (4), pp. 571-582 (1987)

Gross et al. (Gross) "Interferon- α with Condylomata acuminata and Juvenile Diabetes Mellitus," Deutsche Medizinische Wochenschrift, Vol. 111 (36), pp. 1351-1355, (1986) (abstract only)

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Claims 1-4, 6, and 7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins, claim 5 stands rejected under 35 U.S.C. § 103(a) as obvious over the teachings of Cummins, and claims 1-18 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins, Shibutani and either Sobel I or Sobel II (abstract only). In addition, claims 1-7 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of copending application 08/631,470 (the '470 application), and claims 1-18 stand provisionally rejected as claiming the same invention as claims 1-18 of copending application 08/844,731 (the '731 application). Finally, claims 8-18 are the subject of a provisional double-patenting rejection over claims 1-18 of the '470 application in view of the abstracts of Sobel II, Gross, and Giron. After careful review of the record and consideration of the issues before us, we affirm the rejection under 35 U.S.C. § 102(b) as to claims 1-3, 6, and 7, the rejection of claim 5 under 35 U.S.C. § 103(a) over Cummins, the provisional rejections under 35 U.S.C. § 101, and the provisional obviousness-type double-patenting rejection, but reverse the rejection under 35 U.S.C. § 102(b) as to claim 4. In addition, we vacate the rejection of claims 1-18 under 35 U.S.C. § 103(a) over the combination of Cummins, Shibutani, and either Sobel I or Sobel II (abstract only).

BACKGROUND

The invention of the instant application is drawn to the treatment of auto-immune diseases in an animal, including humans, by orally administering a type one interferon to the animal. The interferon may be alpha or beta interferon, and is preferably human recombinant interferon, rat interferon, or murine interferon. See Specification, page 20.

According to the specification, the type one interferon is administered at a dosage that would effectively inhibit the onset or reoccurrence of an autoimmune disease. In addition, a wide variety of auto-immune diseases may be treated according to the invention, "includ[ing] multiple sclerosis, rheumatoid arthritis, diabetes mellitus, psoriasis, organ-specific auto-immune diseases, chronic inflammatory demyelinating polyradiculoneuropathy and Guillain-Barré syndrome." Id. at 21.

DISCUSSION

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Findings of fact and the conclusions of law must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact relied upon in making the rejections are reviewed by the Court of Appeals for the Federal Circuit, or reviewing court, for substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). A determination of whether the findings of fact are supported by the record is difficult to make, however, if the examiner does not explicitly set forth those findings.

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425, 426-7(CCPA 1976). We thus affirm the rejection as it applies to claims 1-3, 6 and 7.³

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sclerosis, appellant further points out that the Cummins patent does not have claims drawn to multiple sclerosis or other autoimmune diseases. See id. at 10.

Appellant also argues that Cummins cannot anticipate the instantly claimed invention because of differences in the route of administration of the interferon. The instant claims require that the type one interferon be "ingested after administration." According to appellant, Cummins requires that the interferon be administered in such a manner so as to have maximum contact with the oral and pharyngeal mucosa. Appellant argues that the instant claims require, citing the 132 declarations of Dr. Lindsey and Dr. Wolinsky, contact with the gastric and intestinal mucosa. In the human studies, appellant asserts, citing the declaration of Dr. Lindsey, that even though there was brief contact with the oral mucosa, the contact was minimal, unlike the contact taught by Cummins, where increased contact is sought. Thus, Appellant contends that Cummins teaches away from the immediate ingestion of interferon, as required by the instant claims. See id. at 12-15.

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Glaug, 283 F.3d 1335, 1338, 62 USPQ2d 1151, 1153 (Fed. Cir. 2002). In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477,

44 USPQ2d 1429, 1432 (Fed. Cir. 1997). During ex parte prosecution, however, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification. See In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

The Cummins reference states that human patients with conditions such as acute rheumatoid arthritis and multiple sclerosis were treated with human alpha-interferon at a dosage of 0.7 IU per pound twice a day. The interferon was retained in the mouth for one minute, and then either swallowed or discharged from the patient's mouth. See id. at Col. 12, lines 14-29.

With respect to the treatment of rheumatoid arthritis, an auto-immune disease, Cummins teaches that:

Two patients suffering from rheumatoid arthritis were treated—a Caucasian male age 44 and a Caucasian female age 44. The male patient was pain free in 7 days, and the female was pain free in 10 days. They were both continued on the oral interferon for 21 days total and have remained asymptomatic.

Col. 12, lines 30-35

With respect to the treatment of a patient with multiple sclerosis, Cummins states:

A 30-year-old Caucasian female nurse afflicted with multiple sclerosis and who had an extensive neurologic workup at City of Hope Hospital in Los Angeles received treatment in accordance with the present invention for 21 days. The patient has had no recurrence of her neurologic symptoms for the past nine months.

Col. 12, lines 40-45.

Thus, Cummins teaches all of the limitations of the claims. Cummins teaches a method of treating an auto-immune disease, such as rheumatoid

arthritis of multiple sclerosis, through the administration of a type one interferon. Appellant's argument that the Cummins reference does not enable the present claims because it presents a single anecdotal example is not found to be convincing. We recognize that in order for a reference to be anticipatory, it must be enabling. See In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962) ("[B]efore any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention."), In re Donohue, 766 F.2d 531, 533, 225 USPQ 619, 621 (Fed. Cir. 1985) (reaffirming LaGrice). However, Cummins clearly states that the symptoms of patients with rheumatoid arthritis and multiple sclerosis were reduced upon treatment of oral interferon. In addition, although appellant's specification may disclose auto-immune diseases not discussed or taught by Cummins, the disclosure of a species anticipates the genus. Cummins teaches the treatment of rheumatoid arthritis and multiple sclerosis, both auto-immune diseases. In addition, although appellant asserts that because Cummins does not claim the treatment of an auto-immune disease, the examiner must have deemed such claims not to be enabled by the specification, appellant presents no evidence to that effect. Finally, just because appellant provides data that was not presented by Cummins, does not render the Cummins reference nonenabling.

The declarations of John William Lindsey and Jerry S. Wolinski have been considered, but are also not deemed to be convincing. Both declarations address whether the claims at issue in this appeal would have been obvious over the Cummins reference. The issue is not one of obviousness, however, but anticipation. In addition, with respect to the comments that one would have not

have had a reasonable expectation of success of practicing the claimed method, Cummins teaches at the very least that the treatment of rheumatoid arthritis patients and a multiple sclerosis patient resulted in the reduction of symptoms, and thus does teach that the method produced the desired result—the treatment of an auto-immune disease.

Appellant's arguments and the statements in the declarations that Cummins cannot anticipate the method claims at issue because of the purported difference in the route of administration of the interferon have also been considered, but are also not deemed to be convincing. The declarations state that the method of Cummins stresses that contact with the oral and pharyngeal mucosa should be maximized, whereas the instant claims require that the interferon be "ingested after oral administration." As noted above, during examination, the claims are to be given their broadest reasonable interpretation. The specification provides no special meaning for the word "ingest." Ingest, however, may be defined as "[t]o take or absorb (food) into the body." The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). The definition of ingest, and the use of the phrase "such that the type one interferon is ingested after oral administration" does not exclude adsorption of the interferon through the oral and/or pharyngeal mucosa as taught by Cummins. Thus, the claims are not limited to a method of delivery wherein contact with the oral or pharyngeal mucosa is avoided.

Appellant also argues that dosages used by Cummins are smaller than the dosages required by the instant invention. Cummins, according to Appellant, administered dosages ranging from 0.01 to 5 I.U. per day, whereas the instant application uses dosages ranging from 5 I.U./kg to about 50,000 I.U./kg.

This argument is not found to be convincing with respect to those claims wherein no dosage is recited, i.e., claims 1-3, 6, and 7. The rejection with respect to claim 4 is reversed, however, as the lower end of the range, i.e., 50 I.U./kg, is higher than the dosage used by Cummins.

2. Rejection under 35 U.S.C. § 103(a) over Cummins

With respect to the rejection of claim 5 as being rendered obvious by Cummins, the examiner states:

The disclosure is the same as above as discussed for claim 1. The patent does not disclose an alternate day dosing. However, it does show that a daily dosage is possible, as a single dosage or as divided and administered in a multiple daily dose regimen. The reference also teaches a staggered regimen of 1-3 days per week or month as an alternative to daily dosing. See col. 5, lines 50-55. With such a flexibility as taught by the reference, and since it is common knowledge in the art to employ such a regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc., it would have been obvious to one of ordinary skill in the art to adopt an alternate day dosing and administer [interferon] as shown by Cummins for [multiple sclerosis].

Examiner's Answer, pages 4-5.

The portion of the Cummins patent relied upon by the examiner states that:

Daily dosage of interferon can be administered as a single dose or, preferably, it is administered in a multiple-dose daily regimen. A staggered regimen, for example one to three days of treatment per week or month, can be used as an alternative to continuous daily treatment.

Col. 5, lines 51-56.

Appellant argues that the first portion of the above passage teaches a multiple-dose regimen rather than an alternate day regimen. In addition, according to appellant, although Cummins discloses a regimen of one to three

days per week or month, that dosing regimen is also "alluded" by Cummins a being a less preferred mode of administration. The specific spacing of treatments is not discussed by Cummins, and thus, appellant contends that it is unclear whether this section refers to three continuous days of treatment, followed by a period without treatment, or single days of treatment separated by days without treatment. See Appeal Brief, pages 18-19. Thus, appellant concludes that the section relied upon by the examiner is non-enabling, as "[u]ndue experimentation would be necessary to try the other possible combinations days on therapy versus days off therapy." Appeal Brief, page 17.

Appellant's arguments are not deemed to be convincing. Cummins teaches a variety of different treatment regimens, from daily to monthly. From those teachings, the ordinary artisan would have concluded that the spacing of the treatments is not crucial to the success of the treatment method. "All the disclosures in a reference must be evaluated, including nonpreferred embodiments, ... and a reference is not limited to the disclosure of specific working examples." In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 199 (CCPA 1972) (citations omitted). As the examiner notes, and appellant does not refute, it is common in the art to use alternate day dosing, and it is irrelevant that such alternate dosing schedules may have been less preferred mode of administration.

In addition, merely because Cummins does not explicitly disclose alternate day dosing does not lead to the conclusion that the reference is not enabled for such dosing. As noted above, alternate day dosing is commonly used in the art, and given the variety of dosing schedules taught by Cummins, the ordinary artisan would have had a reasonable expectation of success that

such an alternate day dosing could be used in the treatment method taught by Cummins.

3. Rejection under 35 U.S.C. § 103(a) over Cummins, Shibanti and Sobel I or Sobel II (abstract only)

Claims 1-18 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins, Shibutani and Sobel I or Sobel II (abstract only). The entire rejection is set forth below.

The disclosure for the patent is as discussed above. The whole range of dosages claimed by the instant invention is not shown. However, the Shibutani abstract indicates that IFN toxicity studies with rats showed that it was tolerated well. Therefore, it would have been obvious to one of ordinary skill in the art to administer dosages higher than that shown in the patent with the reasonable expectation that such doses would not produce toxicity side-effects in humans. It would also have been obvious to employ such an alternate day dose regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc. Note that although Cummins discloses interferon for autoimmune diseases which includes the diabetes claimed herein, the reference does not expressly state that the disease condition is diabetes. However Sobel shows the use of interferon for diabetes and that diabetes was known in the art as an autoimmune disease at the time the invention was made. See col. 8, line 63 to col. 9, line 5 and claims 11-12 and 18.

Examiner's Answer, pages 5-6.

Again, the panel would like note that the examiner has entered a shotgun rejection of all of the claims, rather than performing a claim-by-claim analysis.

The examiner relies upon Shibutani as a teaching dosage amounts over those taught by Cummins may be used, but dosage amounts are only specifically

recited in claims 4, 10, 14, and 18. Moreover, the record is incomplete because the examiner failed to consider the Sobel II reference in its entirety.

Because of the lack of claim-by-claim analysis, and because the rejection did not consider the teachings of Sobel in its entirety, and because it is the opinion of the panel that the Sobel II reference, when considered in its entirety, may be relevant to the patentability of the claims, the rejection over Cummins, Shibutani and Sobel I or Sobel II (abstract only) is vacated. See, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (stating that for meaningful judicial review to occur, the agency must present a full and reasoned explanation of its decision.) Moreover, the panel also notes that the disclosure of Sobel I is not commensurate with the disclosure of Sobel II, as Sobel I is drawn to the use of gamma interferon in the treatment of diabetes, whereas Sobel II is drawn to the use of type one interferon in the prevention and treatment of diabetes.

As a final note, in assessing the prior art, each prior art reference must be considered in its entirety in an obviousness determination. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). In assessing the teachings of the prior art reference as a whole, the examiner must also consider those disclosures that may teach away from the invention. See In re Fine, 837 F.3d 1071, 1074, 5 USPQ2d 1596, 1598 (1988). In this case, Cummins teaches that the amount of interferon should be used in amounts of "less than 5IU/lb of body weight," Col. 3, lines 9-12, and characterizes the method as "using

interferon in low oral dosages," Col. 1, lines 6-14. Thus, may Cummins teach away from using higher dosages, and thus there may be no motivation for increasing the dosage amount of interferon. Thus, Cummins may teach away from a combination that includes Shibutani.

4. Provisional Rejections under 35 U.S.C. § 101

Claims 1-7 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as claims 1-7 of the '470 application. In addition, claims 1-18 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as the '731 application.

Appellant states that should any of the applications be allowed, the claims will either be amended or withdrawn from one of the copending applications. As appellant has not presented any arguments as to why the rejection is improper, it is affirmed.

5. Obviousness Double Patenting rejection

Claims 8-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the '470 application in combination with the abstracts of Sobel, Gross, and Giron. Appellant states that should either application be allowed, a terminal disclaimer will be filed. Again, as appellant has not presented any arguments as to why the rejection is improper, it is affirmed.

OTHER MATTERS

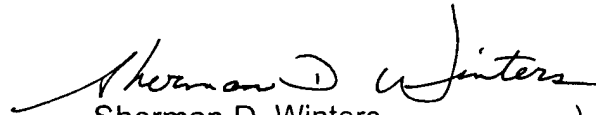
The Sobel II reference, when considered in its entirety, appears to be relevant to the patentability of the claims at issue. Sobel II teaches that autoimmune diseases, such as Type I diabetes mellitus, may be treated or prevented by the administration of an α -interferon or a β -interferon. See Sobel II, page 1. Sobel II teaches the use of different dosages and different administration schedules, and notes that any mammal may be treated, including human. See id. at 7-8. In addition, Sobel II teaches that the interferon may be administered orally. See id. at 8 and 26. Thus, upon receipt of the application, the examiner should consider the patentability of the claims in view of the teaching of Sobel II.

CONCLUSION

The rejection under 35 U.S.C. § 102(b) as to claims 1-3, 6 and 7, the rejection of claim 5 under 35 U.S.C. § 103(a) over Cummins, the provisional rejections under 35 U.S.C. § 101, and the provisional obviousness-type double-patenting rejection, are affirmed. The rejection under 35 U.S.C. § 102(b) as to claim 4, however, is reversed. In addition, we vacate the rejection of claims 1-18 under 35 U.S.C. § 103(a) over the combination of Cummins, Shibutani, and either Sobel I or Sobel II (abstract only). Finally, the examiner may want to consider the patentability of the claims at issue in the appeal of in view of the teachings of the Sobel II reference in its entirety.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

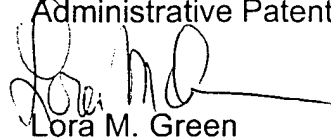
AFFIRMED-IN-PART; REVERSED-IN-PART; VACATED-IN-PART



Sherman D. Winters
Administrative Patent Judge



William F. Smith
Administrative Patent Judge



Lora M. Green
Administrative Patent Judge

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